Author's response to reviews

Title: Peroxisome proliferator-activated receptor gamma and spermidine/spermine N1-acetyltransferase gene expressions are significantly correlated in human colorectal cancer.

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Author’s response to reviews:

Dr. Alison Fairservice
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Dear Madam,

the manuscript "Peroxisome proliferator-activated receptor gamma and spermidine/spermine N1-acetyltransferase gene expressions are significantly correlated in human colorectal cancer" has been modified according to Editor's suggestions. The English has been improved; the informed consent has been included in the manuscript (Methods section, pag. 6, line 5); the acknowledgement section and the source of funding for the study have been indicated. Moreover, the manuscript has been revised taking into account the reviewer's comments.

Reviewer 1 (Debora L. Kramer)
We agree with comment of the reviewer. Further experimentations on this issue to establish the role of PPARg in regulating the SSAT expression and activity are needed in colorectal biology. To date, we are studying the relationship between PPARg and SSAT for a potential implication in the human gastrointestinal disease treatment.

Reviewer 2 (Natalia A. Ignatenko)
Comment - Authors should explain why did they focus on the evaluation of the mutational status of codon 12 and did not analyse codon 13 or 61 mutations ?

Answer - We have focused our attention on the evaluation of the mutated codon 12 of the K-ras since this mutation is mostly frequent (27% - 30%) in colorectal tissue as compared to mutated codon 13 (5% - 6%). Moreover, the mutated codon 61 occurs more frequently in other cancer tissues (1-3). Therefore, the percentages of mutated codon 13 and 61 would be very low in the 40 patients considered in our study (Background section, pag. 5, two last lines)
Reviewer 3 (Francis Raul)

1. Comment - Background, two last lines of page 4: there is an apparent contradiction between the sentence: "Induction of SSAT .... typically gives rise to growth inhibition...." and the following sentence "Moreover, increase SSAT activity has been observed in breast cancer.......".

Answer - We have rephrased and better explained these sentences (Background section, pag. 4, three last lines)

2. Question- In the text of results, discussion and in table 3. The terms mutated K-ras or K-ras negative; K-ras wild-type or K-ras positive are used alternatively and renders the text confusing.

Answer - Throughout the manuscript we have used the terms mutated and non mutated K-ras to indicate the colorectal tissues with and without K-ras mutation, respectively.

Question- How are you excluding that tumor samples may present a mutated K-ras at another location than codon 12?

Answer - Regarding the presence of a mutated K-ras at another location than codon 12, please see answer to reviewer 2.

3. Question- Discussion of pag 10: do the authors mean that an increase of SSAT without a concomitant downregulation of the polyamine biosynthetic pathway (ODC inhibition) is insufficient for counteracting tumor development?.

Answer - This issue has been discussed in greater details and supported by some references in the text (Discussion section, pag. 10, lines 19-23, and pag. 11, lines 1-15)

4. Question- In order to standardize presentation with table 2, values for PPAR mRNA should be presented at the bottom of table 3.

Answer - Values for PPARg mRNA have been presented at the bottom of Table 3

Thank you for your attention to our manuscript.

Yours sincerely
Michele Linsalata, B.D.